THAT WHICH IS CLAIMED IS:

1. A solid gel matrix comprising a solid gel and one or more SERS-enhancing nanoparticles with an attached probe that binds specifically to an analyte.

2. The gel matrix of claim 1 comprising a plurality of the nanoparticles to provide a plurality of unique optical signatures.

3. The gel matrix of claim 2, wherein the SERS-enhancing nanoparticles comprise one or more Raman-active tags independently selected from the group consisting of nucleic acids, nucleotides, nucleotide analogs, base analogs, fluorescent dyes, peptides, amino acids, modified amino acids, organic moieties, quantum dots, carbon nanotubes, fullerenes, metal nanoparticles, electron dense particles and crystalline particles.

4. The gel matrix of claim 1, wherein at least one of the nanoparticles has a net charge.

5. The gel matrix of claim 1, wherein the nanoparticles each provide a unique SERS-signal that is correlated with binding specificity of the probe of the nanoparticle.

6. The gel matrix of claim 1, wherein the Raman-active tag comprises adenine or an analog thereof.

7. The gel matrix of claim 1, wherein the nanoparticles are composite organic-inorganic nanoparticle (COINs) comprising a core and a surface, wherein the core comprises a metallic colloid comprising a first metal and a Raman-active organic compound.

8. The gel matrix of claim 7, wherein the COINs further comprise a second metal different from the first metal forming a layer overlying the surface of the nanoparticle.

9. The gel matrix of claim 8, wherein the COINs further comprise an organic layer overlying the metal layer, which organic layer comprises the probe.

10. The gel matrix of claim 1, wherein the probe is selected from antibodies, antigens, polynucleotides, oligonucleotides, receptors and ligands.

11. The gel matrix of claim 10, wherein the probe comprises a polynucleotide.

12. The gel matrix of claim 1, wherein at least some of the nanoparticles further comprise a fluorescent label that contributes to the optical signature.

13. A method for producing a gel matrix comprising:

a) forming a liquid composition by mixing together

a gel-forming liquid comprising gel-forming particles in a suitable liquid; and

a plurality of Raman-enhancing nanoparticles having a plurality of unique optical signatures, and an attached probe for binding to an analyte; and

b) obtaining a solid gel matrix from the liquid composition.

14. The method of claim 13, wherein the gel matrix comprises a plurality of the SERS-enhancing nanoparticles, each having an attached probe that binds specifically to a known analyte to form a complex.

15. The method of claim 14 wherein the SERS-enhancing nanoparticles are COINs.

16. A method for detecting an analyte in a sample comprising:

contacting a sample containing a analyte with a gel matrix of claim 1 under conditions allowing binding of the probe to the analyte to form a complex;

separating the complex from other sample contents by electrophoresis or magnetophoresis; and

detecting SERS signals emitted by complexes separated at various locations within the gel, wherein a SERS signal emitted by a particular complex is associated with the presence of a particular analyte.

17. The method of claim 16, wherein the gel matrix comprises two or more of the complexes and the signals from the two or more complexes are indicative of the presence of two or more different analytes.

18. The method of claim 16, wherein the SERS signal from a particular complex provides information regarding the chemical structure of the analyte.

19. The method of claim 18, wherein the gel matrix is a polyacrylamide gel and the analytes are selected from antigens, polypeptides, proteins, glycoproteins, lipoproteins, and combinations thereof.

20. The method of claim 16, wherein at least two of the nanoparticles are metal-containing SERS-enhancing nanoparticles having different net charges.

21. The method of claim 20, wherein the SERS-enhancing nanoparticles are COINs.

22. The method of claim 16, wherein the analyte is contained in a biological sample.

23. The method of claim 16, wherein the associating comprises determining a mobility change caused by binding of the probe to the analyte.

24. The method of claim 16, wherein the separating comprises electrophoresis.

25. The method of claim 16, wherein the method further comprising subjecting the analyte to chromatography or isoelectric focusing prior to or following the detecting.

26. The method claim 24, wherein the electrophoresis is one dimensional or two-dimensional electrophoresis under non-denatured conditions.

27. The method of claim 16, wherein the method further comprises soaking the gel in a chemical enhancer solution and drying the gel to concentrate the samples prior to the detecting.

28. The method of claim 16, wherein the sample comprises one or more additional analytes having substantially the same size and/or same charge density and said method comprises associating the optical signals with the identity of the at least one analyte based on altered mobility of the complex in the gel as compared with that of the additional analytes having substantially the same size and/or same charge density in the sample.

29. The method of claim 28, wherein the signals are SERS spectra and the spectra are compared with a SERS database containing SERS spectra of a plurality of analytes to identify bound analytes.

30. The method of claim 29, wherein the SERS spectra of one or more analytes in the sample are compared with a collection of SERS spectra to determine a difference, wherein the difference is associated with a known biological phenotype or disease.

31. The method of claim 16, wherein the sample is a body fluid.

32. The method of claim 31, wherein the sample is blood serum.

33. A system for detecting an analyte in a sample comprising:
a gel matrix of claim 1;
a sample containing at least one analyte; and
an optical detection system suitable for detecting SERS signals from the nanoparticles.

34. The system of claim 33, further comprising a computer comprising an algorithm for analysis of the SERS signals obtained from the sample.

35. A method for multiplex detection of target molecules in a sample, said method comprising:

contacting target molecules in a sample under conditions suitable to allow complex formation of analytes in the sample with a set of probe constructs, each construct comprising a

non-nucleic acid probe conjugated with an optically-active nucleic acid barcode comprising at least one SERS-active nucleotide and having both a unique mobility in electrophoresis and a unique optical signature;

separating the complexes by electrophoresis;

detecting the unique optical signatures in a multiplex manner with a suitable detection device; and

associating individual optical signatures from the constructs with the identity of the corresponding analytes in the sample.

36. The method of claim 35, wherein the unique mobility results from the constructs in the set having varying number of nucleotides in the barcode.

37. The method of claim 35, wherein at least some of the constructs have a net charge.

38. The method of claim 35, further comprising separating free targets and/or free unbound probe constructs from the complexes by electrophoresis.

39. The method of claim 35, wherein the non-nucleic acid probes are antibodies that bind specifically to known protein-containing targets.

40. The method of claim 35, wherein the separated complexes are detected by optical techniques selected from adsorption, reflection, polarization, refraction, fluorescence, Raman spectra, SERS, resonance light scattering, grating-coupled surface plasmon resonance and combinations thereof.

41. A method for making a set of active Raman molecular codes for detecting non-Raman-active analytes, said method comprising:

obtaining a set of molecular backbones, each comprising an organic polymer that contains two or more chemically reactive positions along the backbone;

attaching at least one small molecule Raman-active tag to each backbone in the set at the chemically reactive positions, wherein the type, number and relative position of the Raman-

active tags along the backbones of members of the set are variously combined to produce a unique Raman signal for each member of the set; and

conjugating an active group to the backbones in the set, wherein each active group specifically binds to a known analyte.

42. The method of claim 41, wherein the molecular backbone comprises naturally occurring or synthetic polysaccharides, proteins, amino acids or a combination thereof.

43. The method of claim 42, wherein the backbone is a single stranded or double stranded polynucleotide fragment comprising at least one residue that has been modified for chemical attachment of a Raman-active tag.

44. The method of claim 43, wherein the modified residue is a 2-amino purine.

45. The method of claim 43, wherein the backbone is synthesized by standard phosphoramidite chemistry.

46. The method claim 41, wherein the Raman active tags are selected from a dye or a naturally-occurring Raman active amino acid or nucleic acid.

47. The method of claim 41, wherein the Raman active tag is a series of contiguous nucleic acids and the tag is linearly attached to the polymer backbone by synthesizing the tag on the backbone by standard phosphoramidite chemistry.

48. The method of claim 45, wherein the backbone comprises 2 to 1000 nucleotides.

49. The method of claim 41, wherein the members of the set have a common backbone.

50. The method of claim 49, wherein the Raman-active tags are selected from a Raman-active dye, amino acid, nucleotide or a combination thereof.

51. The method of claim 50, wherein the Raman active amino acid is selected from arginine, methionine, cysteine and combinations thereof.

52. The method of claim 50, wherein the Raman-active nucleotide is selected from adenine, guanine and derivatives thereof.

53. The method of claim 41, wherein at least one member of the set further comprises an enhancer moiety bound to a Raman-active tag or Raman-active backbone to boost intensity of the unique Raman signal.

54. The method of claim 41, wherein the Raman-active tag is poly (G) and the enhancer is an amine group or AmC6.

55. The method of claim 41, wherein the active group is a reactive functional group selected from acrydite™, amine and thiol groups.

56. The method of claim 41, wherein the active group binds specifically to a known target and is selected from an antibody, a receptor, a lectin or a phage-displayed peptide.

57. The method of claim 41, wherein the biological analyte is a protein-containing analyte.

58. The method of claim 57, wherein the protein-containing analyte is selected from an antigen, a peptide, a polypeptide, a protein and a complex containing a protein-containing analyte.

59. The method of claim 41, wherein the backbone is a polynucleotide, the tags are Raman-active nucleotides and the method further comprises attaching the tags linearly to the backbone by standard phosphoramidite chemistry.

60. A method for distinguishing biological analytes in a sample, said method comprising:

contacting a sample comprising a plurality of biological analytes with a set of active Raman molecular codes under conditions suitable to allow specific binding of probes therein to analytes present in the sample to form complexes;

separating the bound complexes;

detecting Raman signals emitted by the active Raman molecular codes in the bound complexes, wherein the Raman signals are indicative of the presence of the known biological analyte in the sample.

61. The method of claim 60, wherein the desired biological analytes are a plurality of different protein-containing analytes and the probes in the set are antibodies wherein each antibody binds specifically to a different known biological analyte.

62. The method of claim 60, wherein the Raman signals are collected to provide a protein profile of the sample.

63. A method for assaying a biological sample, comprising

separating the analytes of the sample on a solid support;

contacting separated analytes with a primary set of active Raman molecular codes of claim 41 so as to allow specific binding of the active Raman molecular codes to one or more protein-containing analytes in the sample to form complexes;

contacting the complexes with a secondary Raman code complex so as to amplify Raman signals produced by the active Raman molecular codes in the complexes;

detecting amplified Raman signals produced by the secondary Raman codes; and

associating detected amplified Raman signals with the presence in the sample of the analyte to which the active agent of the active Raman molecular code specifically binds.

64. The method of claim 63, further comprising collecting amplified Raman spectra from the separated complexes to form a protein profile of the sample.

65. The method of claim 63, wherein the contacting of the secondary Raman complexes involves chemical association between bound members of the set of active Raman molecular

codes and a polynucleotide or oligonucleotide in the secondary Raman codes to amplify the Raman signal.

66. The method of claim 65, wherein the members of the set of active Raman molecular codes comprise a Raman-active oligonucleotide backbone and the secondary Raman complexes comprise a complementary oligonucleotide that hybridizes to the backbone and wherein the method further comprises amplifying the Raman-active oligonucleotide backbone.

67. The method of claim 66, wherein the hybridizing is accompanied by ligation of the hybridized complementary oligonucleotides to form a linear or branched Raman-active complex that amplifies the Raman signals.

68. The method of claim 65, wherein the bound members of the set of active Raman molecular codes comprise a Raman-active polynucleotide backbone with a free hydroxyl group at the 3' end thereof, and the method further comprises exposing the bound complexes to dNTPs in the presence of terminal transferase to form a single stranded Raman-active molecule of hundreds of nucleotides in length that amplifies the Raman signal of the backbone.

69. The method of claim 65, wherein the bound members of the set of active Raman molecular codes comprise a polynucleotide backbone with linear Raman-active nucleic acid tag and a free hydroxyl group at the 3' end thereof, and the method further comprises exposing the bound complexes to dNTPs in the presence of terminal transferase to form a single stranded Raman-active molecule of thousands of nucleotides in length to amplify the Raman signal of the backbone.

70. The method of claim 68, wherein the method comprises varying the dNTPs used to amplify the single stranded Raman active molecules of various of the bound complexes to further vary the amplified Raman signals.

71. The method of claim 69 or 70, wherein the amplification technique is rolling circle amplification.

72. The method of claim 65, wherein the secondary Raman complexes comprise complementary polynucleotides attached to metal nanoparticles that hybridize to the polynucleotides and wherein the amplified Raman signals are SERS signals.

73. The method of claim 72, wherein the metal nanoparticles are selected from silver, gold, copper and aluminum.

74. The method of claim 65, wherein the secondary Raman complexes comprise complementary polynucleotides with attached Raman-active tags and the method further comprises generating dendrimers from the secondary Raman complexes and hybridizing the dendrimers to the polynucleotide backbone to amplify the Raman signal.

75. The method of claim 63, wherein the biological sample comprises a body fluid.

76. The method of claim 75, further comprising collecting the amplified Raman spectra from the amplified Raman signals to obtain a protein profile of the biological sample.

77. A method for determining the presence of an analyte in a pool of analytes, comprising:

a) contacting a pool of analytes with a first set of probes attached to discrete sites on a solid support to form probe/analyte complexes at the discrete sites;

b) contacting the probe/analyte complexes with multiple second sets of active Raman molecular codes wherein each second set utilizes a sub-set of probes of the first set as active agents, to form Raman code-containing complexes;

c) contacting bound Raman code containing complexes in situ with metal ions to cover the Raman-code-containing complexes with a thin layer of metal;

d) detecting SERS signals produced by simultaneously irradiating the bound Raman-code-containing complexes at discrete sites on the solid support with the light source; and

e) associating one or more SERS spectra with the presence of particular analytes in the sample.

78. The method of claim 77, wherein the layer of metal is formed by subjecting a colloidal solution of metal cations to reducing conditions to form metal nanoparticles containing the bound complexes in situ.

79. The method of claim 77, further comprising performing amplification of the polynucleotide backbone in bound Raman code-containing complexes on the solid support prior to c).

80. The method of claim 78, wherein the amplification is PCR™ or rolling circle amplification.

81. The method of claim 77, wherein the associating comprises counting SERS signals from each signal point in the discrete sites to determine the number of signal points with the same signatures.

82. The method of claim 81, wherein the associating further comprises conducting multiplex analysis to classify SERS spectra according to Raman code designs.

83. The method of claim 77, wherein the binders are selected from antibodies, phage-displayed peptides, receptors, nucleic acids, ligands, lectins and combinations thereof.

84. The method of claim 77, wherein the analytes are selected from proteins, gluco-proteins, lipid proteins, nucleic acids, virus particles, polysaccharides, steroids and combinations thereof.

85. The method of claim 77, wherein the pool of analytes comprises samples of body fluids of patients known or suspected of having a disease.

86. The method of claim 85, wherein the method is repeated except that the pool of analytes comprises corresponding samples of normal control patients and the method further comprises comparing SERS spectra obtained from patient analytes with SERS spectra obtained from

analytes of normal control patients to identify a difference, wherein the difference indicates the presence of a disease marker in samples of patients known or suspected of having the disease.

87. The method of claim 77, wherein the probes of the first set are divided randomly to obtain the active agents in the multiple second sets, wherein each Raman code in a single second set is unique to members of the single second set and each of the second sets contains the same set of Raman codes.

88. A method for assaying protein content of a biological sample, said method comprising:

a) obtaining a set of active molecular Raman codes comprising functional groups as active agents;

b) contacting a sample with the set of the Raman-active molecular codes so as to allow chemical attachment of the members in the set with the protein functional groups in protein-containing analytes in the sample to form code/protein complexes;

c) separating the code/protein complexes;

d) detecting SERS signals produced by separated code/protein complexes; and

e) associating the SERS signals with particular protein-containing analytes in the sample.

89. The method of claim 88, wherein the set is a set of three Raman-active molecular codes, each member of the set having one of three active groups selected an amino group, a carboxyl group and a thiol group and an oligonucleotide backbone providing a Raman signature unique to the set.

90. The method of claim 89, wherein each member of the set comprises one of three Raman-active molecular codes selected from poly(dA), poly(dG) and polyd(AG).

91. The method of claim 88, wherein the method further comprises dividing the sample into sub-samples prior to b), repeating b), c) and d) for each sub-sample, and counting the Raman signals from each signal point in all of the sub-samples prior to e).

92. The method of claim 88, wherein the sample is digested prior to being contacted with the active molecular Raman codes.

93. The method of claim 92, further comprising using information obtained from Raman spectra to compile a protein profile of the sample.